REMARKS

A. Request for Reconsideration

Applicants have carefully considered the matters raised by the Examiner in the outstanding Office Action but remain of the opinion that patentable subject matter is present. Applicants respectfully request reconsideration of the Examiner's position based on the following remarks.

B. Claims Status

Claims 21-46 are presented for further prosecution. No amendments have been made herein.

C. Prior Art Rejection

The Examiner has made the following three prior art rejections

(1) Claims 21-43 had been rejected as being unpatentable over a combination of Otake or Castor in view of Sachse and Mackaness;

(2) Claims 21-42, 44 and 45 had been rejected as being unpatentable over a combination of Otake or Castor in view of Sachse and further in view of Klaveness; and

(3) Claim 27 had been rejected as being anticipated by Na.

With respect to prior art rejections (1) and (2), the Examiner had cited Otake and Castor in a previous Office Action dated March 20, 2008 to teach the formation of liposomes using supercritical carbon dioxide. The Examiner recognized that Otake and Castor did not teach forming the liposome with an iodine compound or the inclusion of a water soluble amine compound in the preparation of a liposome, and cited Mackaness or Klaveness. Applicants responded to this point made by the Examiner on March 17, 2008 by submitting a test data in the form of a Declaration of Mr. Nakajima. The Declaration provided test data that showed that the preparation of a liposome including a water soluble non-ionic iodine compound by the use of supercritical carbon dioxide shows surprisingly and unexpectedly superior results compared to conventional practices taught in, for example, Mackaness.

In the present Office Action, the Examiner stated that the test data provided in the Declaration of Mr. Nakajima submitted on March 17, 2008 was ineffective to overcome the prior art rejections made by the Examiner because the comparison of samples C and D demonstrates a 2% difference between the prior art and the invention, and thus is not surprising or unexpected. Applicants traverse this rejection on the grounds that the Examiner has not made a fair comparison between the prior art and the claimed invention. A fair comparison must be a side by

side comparison using the same encapsulated compounds, because different compounds have different degrees of encapsulation. A pharmacological compound has a different functionality than water-soluble non-ionic compounds, with respect to encapsulation.

The Examiner's attention is directed to paragraph 11, which describes the samples to be compared. The proper comparison to demonstrate the increase in inclusion that one of skill in the art would expect is between Samples B and C, which encapsulate the same phosphate. Sample B is the process of Mackaness wherein a pharmacological compound has been used in place of the iodine compound. Sample C is the process of Otake using the same pharmacological compound. Sample B had a proportion of inclusion of 6, whereas Sample C had a proportion of inclusion of 15. Thus, the inclusion of the phosphate of Sample C is 2.5 times better than the inclusion of Sample B.

The proper comparison for demonstration of the unexpected results is Samples A and D, which encapsulate the same amide as a water-soluble non-ionic iodine compound. The water-soluble non-ionic compound encapsulated in Samples A and D has an extremely low inclusion percent. From the results of the comparison of Samples B and C, one of skill in the art would expect that the inclusion of Sample D would be 2.5 times better than Sample A or 1.25 (0.5 x 2.5=1.25).

As can be seen from Table 4, Sample D demonstrated surprisingly and unexpectedly superior results compared to Sample A. Sample A is Example 1 of Mackaness which was tested to determine that the weight percent of iodine compound was 0.5. Sample D is Example 1 of Otake using the contrast medium in Mackaness which was tested to determine that the inclusion rate was 17%. Thus, a comparison between Samples A and D demonstrate an increase by a factor of 34 in the inclusion. An increase by a factor of 34 is surprisingly and unexpectedly superior to Sample D's expected increase by a factor of 2.5. In fact, the difference between the surprising and unexpected increase of a factor 34 and the expected increase of a factor of 2.5 is more than 13 times what was expected. Clearly, one of skill in the art would not expect an increase of more than 13 times of the expected increase of inclusion. Thus, the claimed method of preparing a radiographic contrast medium provides surprising and unexpected results with respect to the weight percentage of the encapsulated substance.

Thus, Applicants submit that the Declaration of March 17, 2008, presents test results that clearly demonstrate that the claimed invention provides surprising and unexpected results compared to the teachings of Otake or Castor in view of Sachse and Mackaness or Sachse and Klaveness.

Turning to prior art rejection (3) above, the Examiner has taken the position that the composition of Na is the same as the composition recited in claim 27. Applicants disagree.

First, Applicants note that Na does not teach a liposome. Rather Na teaches a method of preparing nanoparticles. A liposome has a very specific structure comprising a phospholipid bilayer, and thus is multiphasic. In contrast, the nanoparticles of Na are essentially uniform in structure. Na does not state that his surfactants (phospholipids) form a liposome. Thus, the liposomes of the present invention are dramatically different from the nanoparticles of Na.

Second, the structure of the nanoparticle of Na is completely different from the liposome of the present invention. Na specifically states that the surfactant is adsorbed onto the surface. Adsorption means that the phospholipid adheres to or contacts the surface of the X-ray contrast agent. In contrast, a liposome does not adhere to the surface. Rather, it encapsulates or surrounds the contrast agent. Therefore, the encapsulation of a liposome is at the same time physically and chemically different than the adsorption of a phospholipid onto the surface of a compound. Thus, the adsorption of a phospholipid on a contrast agent and the encapsulation of a contrast agent by a liposome are two distinctly different physical and chemical phenomena.

Thus, Applicants submit that Na does not teach the contrast medium recited in claim 27.

In view of the foregoing, it is respectfully submitted that the claims, as presented herein, are patentable over the references cited by the Examiner, either taken alone or in combination.

D. Double Patenting Rejection

Claims 21, 22 and 26 had been provisionally rejected on the grounds of non statutory obviousness-type double patenting based on claims 1, 4, 6, 8-10 and 19 of copending Application 11/180,849; and claims 21, 22, 25, and 27 had been provisionally rejected on the grounds of non statutory obviousness-type double patenting based on claims 1, 5-8, 10-11 and 14-17 of copending Application 11/187,397.

Applicants hereby request that these rejections be held in abeyance until such time as an indication of patentable subject matter. At that time, the claims can be evaluated to determine if the double patenting rejection is still valid and whether a timely Terminal Disclaimers need be filed.

E. Conclusion

In view of the foregoing, it is submitted that the Application is in condition for allowance and such action is respectfully requested. Should any further fees or extensions of time be necessary in order to maintain this Application in pending condition, appropriate requests are hereby made and authorization is given to Account #02-2275.

Respectfully submitted,

LUCAS & MERCANTI, LLP

By: Donald C. Lucas

Donald C. Lucas, Reg. #31,275
(Attorney for Applicants)
475 Park Avenue South
New York, New York 10016
Tel. # (212) 661-8000
Fax # (212) 661-8002

DCL/cmj/mr